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March 31, 2000

By Hand Delivery

Dockets Management Branch
Food and Drug Administration
5630 Fishers Lane
Room 1061 (HFA-305)
Rockville, Maryland 20852

00 MAR 31 P1:39

Re: Dkt. 99P-4932 – Supplement to Citizen Petition for Clarification of Informal Policy Requiring ANDA Suitability Petitions for Parenteral Drugs in Different Container Sizes

Dear Sir or Madam:

A. Action Requested

In a citizen petition dated November 12, 1999, the undersigned requested the following action:

> This citizen petition requests that the Food and Drug Administration (FDA) clarify its informal policy of requiring suitability petitions for parenteral drugs where the only change from the listed drug is in the size of the container and not in the strength of the drug. The clarification should state that a suitability petition is required only for changes in single-dose liquid parenteral drug container sizes.

99P-4932

Sup.1

(Although the citizen petition did not address powder or other dry forms of drugs for parenteral use, the same general principles would apply, and therefore a suitability petition would be required for "single-dose" containers of such products.)

This supplement to the citizen petition requests additional clarification. Specifically, it requests clarification that different multiple-dose container sizes of parenteral drugs are not different "strengths" for purposes of 180-day Waxman-Hatch generic drug exclusivity.

B. Statement of Grounds

1. The November 12, 1999, citizen petition

The citizen petition dated November 12, 1999, relates to the FDA's informal suitability petition policy for different container sizes of parenteral drugs. The citizen petition explains that the policy appears to be based in part on characterizing container size differences as differences in drug "strength." The citizen petition explains that the size of a parenteral drug container does not correspond with the "strength" of the drug in the container. Rather, the "strength" of a parenteral drug is the amount of active drug ingredient in a specified weight or volume of the drug, expressed as a concentration or as a percentage.

For this reason, the citizen petition concluded, a suitability petition is not an appropriate administrative vehicle for the FDA to review proposed changes in the size of

parenteral drug containers. The citizen petition requested clarification from the FDA that the suitability petition procedure should be applied only to changes in parenteral drug container sizes involving single-dose parenteral drug containers. Those containers are analogous to a dosage unit of a solid oral dosage form drug, such as a tablet of a specified weight of the active ingredient, and can therefore be viewed as an amount of active ingredient in a specified dosage unit of the drug, i.e., as a "strength." The citizen petition requested clarification that the size of a multiple-dose parenteral drug container is not a "strength" of the drug for purposes of the suitability petition policy.

2. This supplement to the November 12, 1999, citizen petition

The November 12, 1999, citizen petition noted the following:

> Because the applicability of several other provisions of FDCA section 505 is based on whether or not an ANDA relates to a distinct drug product, interpreting the term "strength" – one of the defining attributes of a distinct drug product – to apply to different multiple-dose container sizes of parenteral drugs may result in the inappropriate use of these other provisions in situations where there are not, in actuality, different drug products, but only one drug product in containers of different sizes.

One of the provisions of FDCA section 505 that is affected by the concept of drug "strength" is the 180-day Waxman-Hatch generic drug exclusivity provision. That provision provides exclusivity to a "previous application" for "a drug" when that application contains a paragraph IV certification with respect to listed patents. The FDA's current position is as follows:

> The agency has determined that each strength of a drug product can be independently eligible for exclusivity. Applicants may be eligible for a separate exclusivity period for each particular strength of the drug product in an ANDA when each strength refers to a different listed drug. . . . The agency, therefore, has determined that each strength of a drug product is itself a listed drug.

64 Fed. Reg. 42873, 42881-82 (August 6, 1999) (proposed rule, "180-Day Generic Drug Exclusivity for ANDAs").

The issue raised in this supplement to the November 12, 1999, citizen petition does not relate to whether each approved "strength" of a drug product should be regarded as eligible for 180-day exclusivity. The supplement assumes that this is a correct interpretation of the statute. Rather, the issue raised in this supplement is whether different sizes of multiple-dose parenteral drug containers are different "strengths" of the drug when the drug does not differ in the amount of active ingredient in a given volume of the drug, i.e., it does not differ in "strength," as that term is understood in all contexts other than the informal suitability petition policy.

It is the position of this supplement that different multiple-dose parenteral drug container sizes are not different strengths of the drug they contain, and, therefore, that the FDA's interpretation of the FDCA as providing 180-day exclusivity to each "strength" does not apply when the only difference in a parenteral drug is in the multiple-dose container size for which authorization is sought in an ANDA for a drug of one given strength (i.e., concentration) of the active drug ingredient.

Clarification is requested that the FDA agrees with the foregoing position.

The position is legally correct, for the reasons set forth in our citizen petition of November 12, 1999. The "strength" of a parenteral drug does not, as a definitional matter, correspond with the size of the container in which the drug is provided. That is, a parenteral drug with a "strength" of 10 mg/ml has the same "strength" when provided in a 50 ml container as it does when provided in a 100 ml container.

The issue is important. Generic drug exclusivity is economically valuable and has significant effects on generic drug company incentives and competitiveness. The scope of generic drug exclusivity should therefore not be determined by a drug product characteristic that is not an inherent part of the drug product as approved in an ANDA and administered to a patient. The size of a parenteral drug container is not approved in an ANDA in the same way as the "strength" of a drug is approved. Rather, it is authorized, in the same way that the container size of any other product is authorized, e.g., 10 mg tablets in 100, 500, and 1000 dosage unit containers. The container size of a drug in tablet form, and the size of a multiple-dose container of a 10 mg/ml parenteral liquid, is not a defining characteristic of either of those products, and, specifically, it is not the same as the "strength" of the product. Rather, container size is determined by practical factors relating to the convenience of shipping, storing, and dispensing various quantities of a given strength of a drug.

That container size is not a basis for distinguishing parenteral drug "strengths" is reinforced by the fact that different container sizes of parenteral drugs are not consistently identified in the Orange Book, as the November 12, 1999, citizen petition points out. This is not a defect in the Orange Book. It is a function of the fact that drug container size is not the "strength" of a parenteral drug. Of course, when a parenteral drug is provided in a single-dose container, the container volume may be regarded as analogous to the "strength" of a dosage unit of a drug. But the analogy does not fit a multiple-dose parenteral drug container.

The principal factors the FDA cites in its rulemaking document as supporting "strength"-specific generic drug exclusivity do not apply to multiple-dose container sizes of parenteral drugs of the same "strength" (i.e., concentration). Those factors are that ANDA applicants should be encouraged to apply for the maximum number of strengths of a drug and that an ANDA for one strength should not block ANDAs for other strengths.

These factors have to do with making a product expeditiously available in the strength variations that are important to the clinical use of the product. In that context, 10 mg and 20 mg "strengths" of a drug tablet have significance to the physician and to the patient. Similarly, 10 mg/ml and 20 mg/ml strengths of a parenteral drug have significance to the physician and to the patient. But there is no significance to the

physician or the patient in the fact that a 10 mg strength tablet is available in container sizes of 100's and 500's. And there is no significance to the physician or the patient in the fact that a 10 mg/ml strength parenteral drug is available in 50 ml and 100 ml multiple-dose containers.

Accordingly, the FDA should clarify that multiple-dose parenteral drug container size is not a "strength" for 180-day generic drug exclusivity purposes. This supplemental citizen petition is not a comment on the proposed rule cited above. That proposal addresses only the relationship between 180-day generic drug exclusivity and an ANDA for a particular "strength" of a drug. The proposal does not address the question of what "strength" means in the context of parenteral drug container sizes.

C. Environmental Impact

A claim for categorical exclusion from the requirements for Environmental Assessment is made pursuant to 21 C.F.R. § 25.31(a).

D. Economic Impact

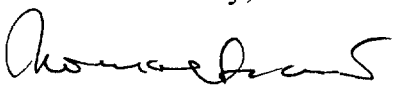
Provided on request.

E. Certification

The undersigned certifies that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies,

and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

Sincerely,



Thomas Scarlett

TS/eam